

## Treatment of Genito-Urinary Tuberculosis With Streptomycin and Synergistic Drugs

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### SUMMARY

*The use of newer drugs in the treatment of genito-urinary tuberculosis is usually auxiliary to accepted surgical and medical procedures. The treatment of choice is removal of the tuberculous focus by surgical methods whenever this can be achieved. Risk of tuberculous complications of surgical operation may be greatly reduced by the use of these drugs. There is also a significant place for such treatment when disease is too far advanced to permit surgical removal. Under these conditions, the principal result is one of palliation only in many circumstances. The drugs of choice at this time are a combination of streptomycin and para-aminosalicylic acid (PAS) and the treatment is frequently more prolonged than in the case of tuberculosis of other organs.*

THE most significant recent practical developments in the field of antibacterial therapy of tuberculosis include: (1) The demonstration that para-aminosalicylic acid (PAS) is an effective and useful auxiliary remedy, and the widespread availability of this drug in a variety of acceptable formulations, (2) the repeated confirmation of the superior therapeutic value of streptomycin when combined with PAS, especially in delaying the development of bacilli which are resistant to either drug, (3) the apparent continued effectiveness of combination therapy for periods of time far in excess of that realized when streptomycin was used alone, (4) the possibility that streptomycin may at times retain some degree of beneficial action even after the tubercle bacilli appear to have become resistant to the drug as judged by laboratory tests, (5) the perfection of methods for parenteral administration of PAS in doses far in excess of those tolerated by the oral route, and with correspondingly enhanced therapeutic efficacy. All of these developments are of paramount significance in a disease so stubborn, so protracted, and so likely to recur as is tuberculosis of the genito-urinary tract.

For less than critical tuberculous infection, a therapeutic regimen employing PAS in doses of 12.0 gm. per day by mouth, combined with 1.0 gm. of streptomycin or dihydrostreptomycin injected intramuscularly two or three times per week, appears to

be adequate to keep the disease process in check. The practical advantages of such a regimen, especially with regard to patients who are not confined to a hospital, is instantly obvious. Such a therapeutic program may be persisted in for long periods, often for many months, before the predominant bacteria appear to have become resistant either to streptomycin or to PAS. While no large series of patients with tuberculosis of the genito-urinary tract has been subjected to such therapy, the author has observed results in a sufficient number of cases to be convinced of genuine therapeutic accomplishments by this means. It is believed, however, that in certain acute and critical, rapidly progressive types of tuberculous infection, daily administration of streptomycin or dihydrostreptomycin may be necessary.

It is doubtful if there is any circumstance in which streptomycin should be employed without PAS in the treatment of tuberculosis, except when persisting severe allergic reaction to PAS makes administration of that drug impossible. The troublesome gastrointestinal irritation produced by PAS usually can be controlled by regulation of the dosage or by shifting to a different formulation, usually some form of the sodium salt combined into tablets or into coated and flavored granules. Fortunately drug tolerance often improves slowly and much depends upon the patient's zeal and fortitude and upon the physician's insistent encouragement and determination.

The protracted discussion concerning the relative toxicity of streptomycin and dihydrostreptomycin loses practical significance when the interrupted combined treatment regimen described earlier in this presentation is employed. When either drug is injected but twice or three times a week, toxic properties are rarely manifested. There is increasing evidence that daily streptomycin administration will produce vestibular damage of mild degree in a small but significant percentage of patients treated for many months. Also there are increasing numbers of reports of delayed damage to the auditory nerve when dihydrostreptomycin is employed in large doses for very long periods. These reports vary so widely that suspicion is growing that not all products labelled as dihydrostreptomycin were identical products, especially during the early months of the development of this drug. There is no convincing evidence that either streptomycin or dihydrostreptomycin possesses any superior therapeutic potency when the two are compared.

Antibacterial drugs other than the streptomycin drugs and PAS have not become established as suitable for the treatment of genito-urinary tract tuber-

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culosis. Derivatives of diaminodiphenylsulfone, of chaulmoogra oil, and of the thiosemicarbazone radical have been suggested but have not appeared to be equal to the PAS-streptomycin combination in treatment of this condition. Viomycin is being studied extensively at present but its present form offers certain disadvantages which make it appear to be an improbable successful contender in competition with PAS and streptomycin. However, it cannot be judged critically upon the meagre data available.

In nearly all instances those forms of genito-urinary tract tuberculosis which, before the advent of streptomycin and PAS, were regarded as necessitating surgical treatment are still so regarded. Furthermore, antibacterial therapy has strengthened the surgeon's approach to many forms of tuberculosis, has widened the range of application of surgical treatment, and has been at least of great palliative value in many circumstances in which, formerly, surgical treatment might have been regarded as a failure.

The availability of additional dynamic therapeutic procedures has made the diagnosis of genito-urinary tract tuberculosis of greater importance and has sharpened interest in the organs of the genito-urinary tract among physicians who care for tuberculous patients. Precise diagnosis and evaluation, such as can only be realized through thorough study by skilled urologists, has become essential whenever the tuberculous patient has urologic symptoms or whenever significant pyuria or microscopic hematuria is noted in routine urinalysis.

Destructive lesions of long-standing tuberculous infection frequently necessitate surgical extirpation when they are so localized as to be subject to removal at reasonable risk, and similar general rules apply whether the seat of the disease be in a lung

or in a kidney. Mucous membrane implants, whether in the bladder, the larynx or the intestine, frequently respond most dramatically to adequate antibacterial therapy with relief of the distressing symptoms caused by such superficial lesions of sensitive mucosal surfaces. In the case of tuberculous cystitis the therapeutic objective frequently is palliation and the prevention or retardation of development of the contracted, low capacity, fibrotic bladder. This may be achieved frequently even when smouldering renal tuberculosis remains, and fortunately such renal infection may at times be compatible with many years of comfortable and productive life.

No discussion of genito-urinary tract tuberculosis is complete which does not stress the metastatic character of the disease and which does not urge the physician and the surgeon to search repeatedly for other foci of tuberculosis, and to employ all hygienic measures which may avoid further dissemination of the disease. Few patients with renal tuberculosis die of renal insufficiency; more commonly the fatal episode is due to tuberculosis elsewhere. Skeletal tuberculosis is peculiarly inclined to develop in association with renal tuberculosis.

The antibacterial drugs were recognized at once as offering real hope to patients with tuberculosis of the genito-urinary tract, but experience eventually produced many disappointments. These failures were usually attributable to the too brief period of effective action of streptomycin, because of the development of resistant bacilli, in so protracted a disease. With newer auxiliary drugs for treatment of streptomycin-resistant strains of bacilli, and with newer regimens of combined therapy which prolong the period of effective antibacterial activity, the future appears brighter than at any previous time.

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